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Original Article

Sensitization according to skin prick testings in atopic patients with asthma or rhinitis at 24 allergy clinics in Northern Europe and Asia

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Abstract

Skin prick tests (SPT) were performed on 2113 atopic patients (407 children and 1706 adults) with asthma and/or rhinitis at 24 allergy clinics in Iceland, Norway, Denmark, Sweden, Estonia, Lithuania and Russia. Test extracts were *Dermatophagoides pteronyssinus* (*D. pteronyssinus*), *Dermatophagoides farinae* (*D. farinae*), cat, dog, horse, birch, timothy, mugwort, Cladosporium, Alternaria, cockroach, chironomids (red mosquito larvae, RML) and shrimp. Among the allergens, timothy followed by cat, birch and dog gave the highest number of positive SPT. Positive SPT with house dust mites (HDM), furred animals, RML and Cladosporium were more common in asthmatics than in patients with rhinitis; birch and timothy more common in patients with rhinitis. Sensitization against *D. pteronyssinus*, horse, timothy and Cladosporium was more common in men than in women. Although the general sensitization pattern of the atopic patients at the participating centers showed similarities, there were also significant differences between centers. Positive SPT with furred animals were most prevalent in Northern and Central Sweden and St Petersburg, and least common in Siberia and Denmark. Pollen allergy was most common in Novosibirsk and on the west coast of Sweden, and less common in Vladivostok. Sensitization against HDM was most common in Lithuania and least prevalent in Northern Sweden and Finland. Insect allergens gave the most positive reactions in St Petersburg and the least positive reaction in Novosibirsk. Sensitization against multiple allergens was found in 74% of the patients and a mono-allergy in 26%. The degree of atopy was higher in males than in females and higher in asthmatics than in patients with rhinitis. The month of birth of the patients did not influence significantly the test results. It is concluded that although the sensitization pattern shows similarities in different regions, it is also influenced to some extent by residence as well as by diagnosis, sex and age of the patients.

Key words: allergic rhinitis, allergy, asthma, hypersensitivity, insects, multicenter, skin test.

Introduction

Sensitization to inhalant allergens is dependent on heredity and environment. The prevalence of asthma and rhinitis varies between countries,[1] and within some countries the prevalence increases the further north the patient is living.[2] However, the degree of sensitization among those with symptoms of asthma and/or rhinitis is difficult to compare between centers as the testing methods vary considerably (e.g. skin tests), or are expensive (e.g. *in vitro* assays). Thus, there are no previous comparative reports on the prevalence of sensitization to common inhalant allergens among patients with asthma and/or rhinitis in various parts of Northern Europe and Asia, and only a few studies comparing different regions with different environmental conditions using the same technique.[1] The availability of standardized skin prick extracts, however, now makes it possible to compare the allergy panorama of many different regions.

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In this paper we report the distribution of sensitization against inhalant allergens and shrimp, evaluated from skin prick tests (SPT) performed in a standardized manner at 24 allergy centers in eight countries in Northern Europe and Asian parts of Russia, and evaluated the influence of residence, age, sex, and month of birth on the sensitization pattern.

Patients and Methods

Patients

The study includes 2113 atopic individuals from 24 allergy centers. There were 1001 males and 1112 females; 407 children (aged 4–16 years) and 1706 adults (aged 17–60 years). Their mean age was 28 years (range 4–60 years). Their diagnoses were asthma in 696, rhinitis in 1064 and asthma + rhinitis in 492 cases.

This study was a purely clinical one: the patients were not randomly selected from the population but were, at each of the 24 centers taking part in this study (Table 1, Fig. 1), consecutive atopic patients referred for routine allergy evaluation because of asthma and/or rhinitis. Because consecutive patients, and only atopic ones, were included, it was felt that they were representative of the atopic patients with asthma/rhinitis at each region. The study commenced in autumn 1993 and was completed in autumn 1994.

According to the protocol of the study, at least 100 atopic patients aged 4–60 years, should have been included from each center. For practical reasons some centers could not fulfil this goal (Table 1)

Table 1. Positive skin prick tests (%) with 13 allergens at 24 allergy clinics

Clinic	No. patients	DP	DF	Horse	Dog	Cat	Timothy	Mug-wort	Birch	Clado-sporium	Alter-naria	RML	Cock-roach	Shrimp
Clinics with adult patients														
Reykjavik (I)	91	18	12	20	27	56	58	10	9	1	1	2	19	8
Aarhus (D)	83	39	28	13	21	36	46	17	43	2	7	17	31	13
Tromsö (N)	71	23	n.d.	19	47	58	63	7	39	3	n.d.	10	18	17
Göteborg, AD (S)	136	18	15	21	27	39	52	25	78	3	5	4	10	9
Halmstad, AD (S)	107	30	29	20	38	44	56	16	52	2	7	16	28	23
Malmö (S)	97	31	30	14	47	58	65	28	53	4	8	4	14	19
Örebro (S)	106	12	9	29	54	59	52	22	42	6	6	13	22	17
Falun (S)	57	18	12	28	39	67	67	21	56	9	4	11	23	18
Uppsala (S)	89	12	10	21	43	66	52	23	56	5	3	8	19	10
Stockholm (S)	117	21	14	29	41	56	50	15	54	3	3	4	11	15
Umeå, AD (S)	80	9	13	34	58	66	44	9	58	6	5	15	15	18
Boden (S)	80	8	n.d.	24	44	63	37	n.d.	44	6	n.d.	9	14	8
Helsinki (F)	49	8	12	16	35	43	41	27	47	2	2	18	18	8
Tallinn (E)	102	28	23	14	36	38	42	33	42	2	2	5	12	2
Tartu (E)	89	29	24	11	36	43	30	32	32	1	6	8	24	12
St Petersburg (R)	78	17	12	17	50	60	32	26	27	1	3	10	41	21
Moscow (R)	89	18	11	16	36	53	41	34	28	3	5	12	29	16
Novosibirsk (R)	97	16	9	6	14	26	50	44	47	0	4	4	16	7
Clinics with children														
Göteborg, CH (S)	51	20	16	39	41	65	55	20	51	12	2	10	16	10
Halmstad, CH (S)	92	48	42	26	46	48	71	20	54	12	11	8	13	8
Umeå, CH (S)	122	4	3	34	48	69	56	8	43	7	3	6	12	9
Clinics with both children and adult patients														
Nizhne-Kamenka (R)	49	20	12	16	12	22	16	18	20	0	0	2	8	6
Vladivostok (R)	83	33	42	8	21	29	17	22	11	7	10	5	21	13
Klaipeda (L)	98	57	38	19	33	30	40	27	26	6	5	15	28	25
Total	2113	23	19	21	37	50	48	22	43	4	5	9	19	13

CH, paediatric clinic; AD, clinic for adults; D, Denmark; E, Estonia; F, Finland; I, Iceland; L, Lithuania; N, Norway; S, Sweden; R, Russia; DP, *Dermatophagoides pteronyssinus*; DF, *Dermatophagoides farinae*; RML, red mosquito larvae.

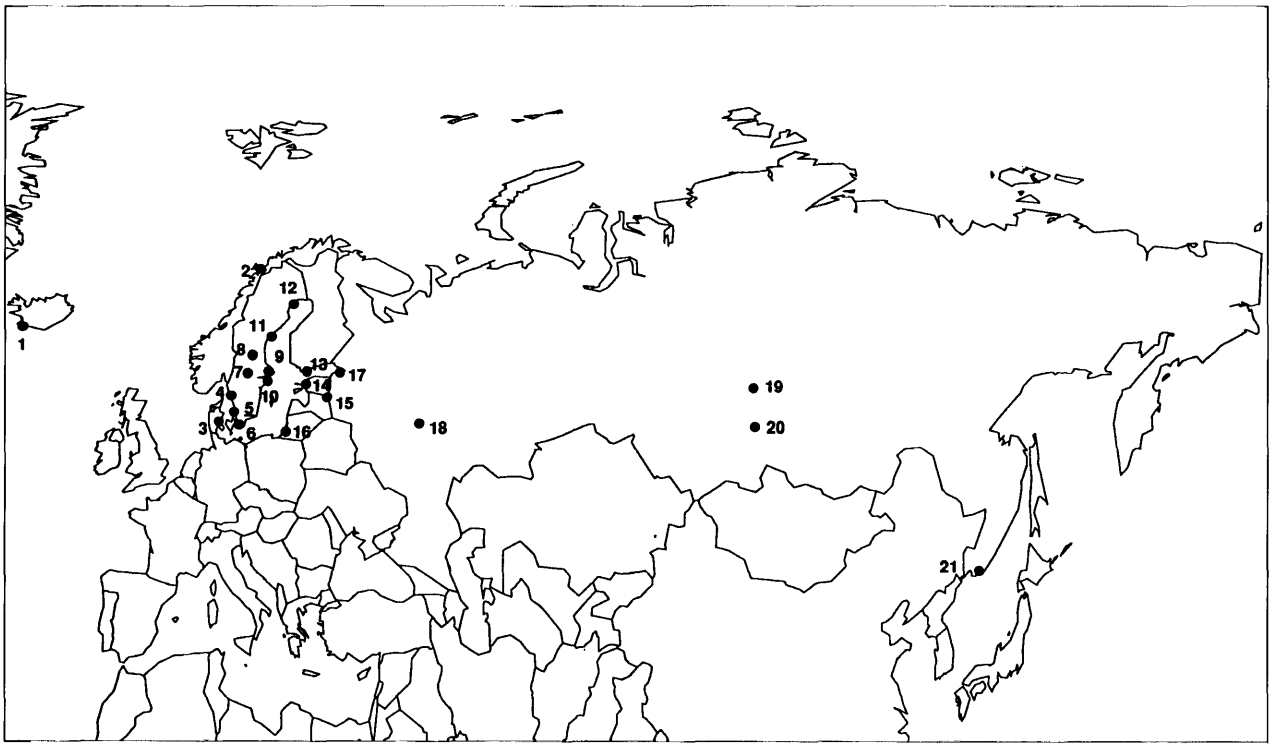

Fig. 1 Locality of participating clinics. 1, Reykjavik, Iceland; 2. Tromsö, Norway; 3, Aarhus, Denmark; 4, Göteborg, Sweden;* 5, Halmstad, Sweden;* 6, Malmö, Sweden; 7, Örebro, Sweden; 8, Falun, Sweden; 9, Uppsala, Sweden; 10, Stockholm, Sweden; 11, Umeå, Sweden;* 12, Boden, Sweden; 13, Helsinki, Finland; 14, Tallinn, Estonia; 15, Tartu, Estonia; 16, Klaipeda, Lithuania;** 17, St Petersburg, Russia; 18, Moscow, Russia; 19, Novosibirsk, Russia; 20, Nizhne-Kamenka, Russia; 21, Vladivostok, Russia. *One clinic for adults and one clinic for children; **patients from two other towns (Vilnius and Siauliai) were also included.

When this study was planned in 1992, relations between allergists in Western Europe and Eastern Europe were few. The allergy centers participating in the present study were chosen because the study co-ordinator had a personal knowledge of these clinics and physicians. The participating centers represented various climatic regions (Fig. 1) and the patients came from large cities (e.g. Moscow) and smaller towns (e.g. Falun), as well as from pure rural regions (Nizhne-Kamenka). In the towns of Göteborg, Halmstad and Umeå, one clinic testing only adults and one testing only children took part. At Klaipeda, Nizhne-Kamenka and Vladivostok both adults and children were included. At all other centers only adults were included. At Klaipeda, patients from two other Lithuanian towns (Vilnius and Siauliai) were included.

The patients were asked about their residence and were accordingly divided into urban patients (living in cities, towns or villages) and rural patients (living in the countryside).

Skin test

Skin prick tests (SPT) were performed on the volar sides of the forearms in accordance with international recommendations.[3] A drop of allergen was placed on the skin, and a prick test lancet with a 1 mm point was inserted through the drop. The wheal reactions were read after 12–15 min. The contours of the reactions were outlined with a pen and transferred to records on a transparent tape. The diameters of the wheals were then measured. Since test results between different centers were to be compared, it was of importance to record the results in a way that could minimize differences in test techniques. The reactions were thus recorded in accordance with the recommendations of the Standardization Committee of the Northern Society of Allergology.[4] A wheal reaction of the same size as that of a histamine reference was recorded as three plus (3+). A wheal with an area double that of 3+ was recorded as 4+ and a wheal double the size

of 4+ was recorded as 5+. A wheal half the size of 3+ was recorded 2+. As a positive reference histamine HCl 10 g/L was used.

In accordance with clinical practice in several northern allergy clinics, the relation between the area of the allergen induced wheals and that of the positive control, and thus the recording of the number of plus signs, was visually judged with the aid of a special skin test ruler. These measurements were taken at the coordinating center (Halmstad).

With each allergen, as well as with the negative and positive controls, double testings were performed at most of the participating clinics. A few centers (e.g. Reykjavik, Aarhus, Tromsö, Göteborg, Boden and the paediatric clinic in Halmstad) chose to perform only single testings, for practical reasons.

When the results of the two tests differed, the largest one was used for the calculations.

At most of the centers, the staff performing the SPT had been accustomed to the test method for several years. At the centers in Estonia and Russia, however, SPT had not been previously used. Before the start of the study, the coordinator met the Estonian and Russian participants and demonstrated the test technique.

Allergen extracts used in skin tests

In the skin testings, extracts of 12 different inhalant allergens and one food allergen (shrimp) were used. The shrimp extract was included because of our interests in cross-reactions between inhalant insect allergens and crustaceans.[5]

Standardized glycerinated allergen extracts (Soluprick SQ, with an activity of 10 HEP, histamine equivalent prick) from Allergy Laboratory, Copenhagen, Denmark (ALK), were used with *Dermatophagoides pteronyssinus* (*D. pteronyssinus*), *Dermatophagoides farinae* (*D. farinae*), horse, dog, cat, birch, timothy and mugwort. The standardization of Soluprick SQ extracts was performed by means of a combination of methods.[6] The first step was a control of the composition of the extract by means of crossed immunoelectrophoresis (CIE) and crossed radioimmunoelectrophoresis (CRIE). The second step was measurement of one or more major allergenic components by means of quantitative immunoelectrophoresis. The final step was a control of the total biological activity.

Commercially available non-standardized extracts were used with Cladosporium and Alternaria (Soluprick 1/20 w/v from ALK) and with cockroach (whole body extracts of German and American cockroaches) and shrimp (genus *Peneus;* 1/10 w/v from Bayer, Spokane, WA, USA). Furthermore, we used extracts of red mosquito larvae (RML), 1/100 w/v, produced by Allergy Laboratory, Sahlgrenska Hospital, Göteborg, Sweden, as earlier described.[5]

At the centers in Tromsö and Boden, *D. farinae* and Alternaria were excluded from the allergen panel. At Boden mugwort was excluded.

Definitions

Patients having symptoms regarded as asthmatic, that is dyspnea, wheezing on exposure to allergens, irritants etc. or showing a reversible airways obstruction on spirometry, were regarded as having bronchial asthma. Patients with a history of continuous or intermittent blockage, sneezing, running or itching, or symptoms of conjunctivitis not caused by infection, were given a diagnosis of allergic rhinitis. Three diagnostic groups were thus included: patients with asthma, patients with rhinitis, and those with both asthma and rhinitis.

In this study, patients having one or several SPT reactions ≥ 2+ with the test extracts were regarded as atopics. Patients having positive reactions with only one of the allergens were regarded as having a mono-allergy. Patients with two or more positive reactions were regarded as having a multi-allergy. The degree of atopy was recorded as the sum of the number of plus signs for 13 allergens (*D. pteronyssinus*, *D. farinae*, horse, dog, cat, birch, timothy, mugwort, Cladosporium, Alternaria, RML, shrimp and cockroach) in each subject.

In some analyses (see results), test results with *D. pteronyssinus* and *D. farinae* were combined into one group, house dust mites (HDM); cat, horse and dog to one group, furred animals (or mammals); birch, timothy and mugwort to pollens; and cockroach and RML to insects. Furthermore, HDM, insects, shrimp, Alternaria and Cladosporium were combined to a group called arthropods and moulds. When an SPT was positive with any of the allergens in the group, the test with the allergen group was regarded as being positive.

Statistical methods

SPSS statistical software was used in the statistical analysis. The Spearman's correlation coefficient was used for analysis of linear relationship. For comparison between groups the Chi-squared test and the Mann–Whitney *U*-test were used. Multivariate logistic regression analysis was used when taking several independent variables (clinic,

sex, age and diagnosis) into account. Values of $P < 0.01$ were considered significant. All tests used were two-tailed. The study was approved by the Ethics Committee in Lund, Sweden.

RESULTS

Sensitization pattern

The highest number of positive SPT in the atopic patients were found with cat (50%), timothy (48%), birch (43%) and dog (38%) (Fig. 2). With dog allergen a higher proportion of weak reactions (1+) were found than with other allergens.

According to allergen groups, 1475 (70%) of the atopic patients had an allergy against pollen, 1280 (61%) had an allergy against furred animals and 457 (22%) had an allergy against insects. Concomitant sensitization against mites, insects and moulds was found in 893 (42%) of the cases, while concomitant sensitization against furred animals and pollen was found in 897 (42%) of the patients.

Sensitization at different clinics

Although the sensitization pattern at the different centers on the whole showed similarities, there were with all of the allergens, except Alternaria, significant differences between the clinics taking part (Table 1).

Sensitization against furred animals was most common in Northern and Central Sweden, Tromsö and St Petersburg, and least common in Siberia and Aarhus. Thus, 69% of the atopic children in Umeå were sensitized against cat as opposed to only 22% in Nizhne-Kamenka. Positive SPT with dog were found in more than 50% of the patients in Umeå, Örebro and St Petersburg but in less than 15% of the patients in Novosibirsk and Nizhne-Kamenka. Sensitization against horse was frequent in children in Göteborg and Umeå and least common at the Siberian clinics.

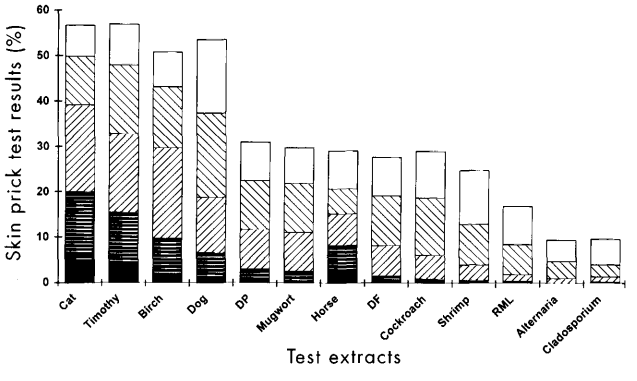

Fig. 2 Sensitization pattern in 2113 atopic individuals with asthma and/or rhinitis. ■>4+ ▤4+ ▨3+ ▧2+ □1+. DP, *Dermatophagoides pteronyssinus;* DF, *Dermatophagoides farinae;* RML, red mosquito larvae.

Pollen allergy was most prevalent in Novosibirsk and at the centers on the west coast of Sweden (80–90%) and least common in Vladivostok (31%). Of the individual pollen allergens used, birch pollen gave a positive SPT in 78% of atopic adults in Göteborg and in only approximately 10% in Vladivostok and Reykjavik; timothy showed a positive SPT in more than 70% of the children in Halmstad but in only 16% in Vladivostok and Nizhne-Kamenka; and mugwort showed the highest figures in Moscow (44%) and the lowest in Tromsö, Reykjavik and at the northern Swedish clinics (7–10%).

The figures for sensitization against HDM were highest at the clinics in Lithuania (> 60%) and lowest in the Northern Swedish centers as well as in Helsinki (7–14%). Some differences were noticed when the SPT with *D. pteronyssinus* were compared with those with *D. farinae*. Thus, *D. pteronyssinus* gave the most positive results in Klaipeda (57%) and *D. farinae* the highest results among children in Halmstad (42%). Positive SPT were more often found with *D. pteronyssinus* than with *D. farinae,* the most pronounced difference between positive *D. pteronyssinus* and *D. farinae* was found in Klaipeda.

The insect allergens gave positive reactions most often in St Petersburg (46%) and least often in Novosibirsk (10%). SPT with cockroach were positive in 41% of the cases in St Petersburg as opposed to only 8% in Nizhne-Kamenka. SPT with RML showed the highest figures in Helsinki (18%) and the lowest in Reykjavik and Nizhne-Kamenka (2%). Sensitization against shrimp was most frequently found in Klaipeda (24%) and least often in Tallinn (2%).

The moulds, Cladosporium and Alternaria, showed the highest number of positive SPT among children in Halmstad (12% and 11%, respectively) and the lowest (0%) in Novosibirsk. When the SPT reactions of arthropods (HDM, insects and shrimp) and moulds were grouped together, Vladivostok and Klaipeda showed the highest number of positive SPT with one or more of the included allergens (78% and 73%), and Boden and Umeå, in Northern Sweden, showed the lowest (21% and 22%).

Because the proportion of patients having asthma and rhinitis varied among the clinics, separate analyses were done on the subgroups of patients having asthma, rhinitis, and asthma + rhinitis, respectively. In asthmatic patients

significant differences ($P < 0.01$) between clinics were found with all the allergens except shrimp, RML, Alternaria and Cladosporium; and in patients with rhinitis with all allergens except Alternaria. In the smaller group of patients with both asthma and rhinitis significant differences between clinics were recorded with all allergens except insects, molds and shrimp.

Mono/multi-allergy, number of positive tests and degree of atopy

Among the atopic patients, the mean number of allergens giving positive test results was three. A mono-allergy occurred in 26%, while 21% were sensitized against two allergens, 19% against three, 16% against four and 18% against five or more allergens.

Mono-allergy among patients having positive SPT with the corresponding allergen was most common with birch (16%), cockroach (13%) and timothy (11%), and least common with dog (3%) and horse (3%).

Mono-allergy was significantly ($P < 0.001$) more common in some centers than in others. Thus, 59% of the atopic patients in Nizhne-Kamenka had a mono-allergy as opposed to only 15% of those in Malmö. The number of positive tests varied among centers, from a mean number of 1.5 (median 1) in Nizhne-Kamenka to a mean of 3.9 (median 4) in children in Halmstad.

A measure of the degree of atopy was obtained by adding for each of the patients the number of plus signs obtained by each of the 13 allergens. Scores between 2 and 47 were recorded. Males showed a higher degree of atopy (mean 9.7, median score 9) than females (mean 8.5, median score 8; $P < 0.001$). Asthmatic patients and patients with asthma and rhinitis had a higher atopy degree (mean 10.0 and 10.3, median 9) than patients with rhinitis (mean 8.8, median score 7; $P < 0.001$).

The proportion of mono-allergics increased from 23 to 36% and the mean number of positive tests decreased with age from 3.3 (SD 2.0) to 2.5 (SD 1.6) after the age of 30. The mean degree of atopy decreased from 10.4 (SD 6.6) in patients 20–29 years of age to 7.4 (SD 5.1) in those 50–60 years of age.

Sensitization in relation to diagnosis, age and sex

In asthmatic patients, sensitization with HDM ($P < 0.01$), furred animals ($P < 0.001$), RML ($P < 0.01$) and Cladosporium ($P < 0.01$) was significantly more common than in patients with rhinitis, whereas sensitization against timothy and birch was more common in patients with rhinitis ($P < 0.001$) than in those with asthma.

Among atopic patients, the incidence of positive SPT reactions showed a decrease with age with *D. pteronyssinus* (from 28 to 16%; $P < 0.001$), *D. farinae* (from 24 to 16%; $P < 0.01$), horse (from 26 to 16%; $P < 0.001$) and Cladosporium (from 7% in the youngest age group to 4% in the older age groups; $P < 0.01$). The relative importance of mugwort increased with age (from 14 to 26%; $P < 0.001$). Positive SPT with cockroach were found in 20% of the adults and in 15% of the children (NS).

A separate analysis was performed including the six Swedish clinics, who tested either children only or adults only (Halmstad, Göteborg and Umeå, Table 1). Among 323 adults, SPT with birch were positive in 64% as opposed to only 49% of 265 children ($P < 0.001$). With cat, the positive test results were more common in children (61%) than in adults (48%; $P < 0.01$). SPT with Cladosporium also showed positive results more often in children (9%) than in adults (3%; $P < 0.01$).

Sensitization against *D. pteronyssinus*, horse, timothy and Cladosporium was more common in men than in women ($P < 0.01$). The figures in males and females were 25 and 20% with *D. pteronyssinus*, 23 and 19% with horse, 51 and 45% with timothy and 6 and 3% with Cladosporium.

Sensitization in relation to residence

Because most of the participating clinics included mainly or only urban patients (and one, Nizhne-Kamenka, only included rural patients), an analysis regarding the influence of the residence of the patients on the SPT results could not be meaningful if all centers were to be included in the analysis. For this reason, calculations were performed including only nine clinics, each having at least 15% rural patients. Among these 649 urban and 140 rural individuals, no significant differences were found, although the figures for positive SPT with *D. pteronyssinus*, *D. farinae* and Cladosporium were higher in rural patients and those with horse, cat, dog, timothy and Alternaria were higher in urban ones (NS).

Influence of clinic, sex, age and diagnosis according to multivariate analysis

When the influence of several independent variables on the test results was taken into account, the results shown in Table 2 were found. The testing clinic, that is geographical factors, significantly influenced the SPT results

Table 2. Significances of relationships between test results with the different allergens and clinic, sex, age group and diagnosis, according to multivariate logistic regression

Allergen	Clinic	Sex	Age group	Diagnosis
Cat	$P < 0.001$	$P < 0.05$	$P < 0.05$	$P < 0.001$
Dog	$P < 0.05$			$P < 0.001$
Horse	$P < 0.001$	$P < 0.05$	$P < 0.01$	$P < 0.001$
Timothy	$P < 0.001$	$P < 0.001$		$P < 0.001$
Birch	$P < 0.001$			$P < 0.001$
Mugwort	$P < 0.001$		$P < 0.001$	$P < 0.01$
DP		$P < 0.05$	$P < 0.01$	$P < 0.001$
DF			$P < 0.01$	$P < 0.01$
Cockroach			$P < 0.05$	$P < 0.01$
RML		$P < 0.05$		$P < 0.01$
Cladosporium		$P < 0.01$	$P < 0.05$	$P < 0.001$
Alternaria				
Shrimp		$P < 0.05$		

DP, *Dermatophagoides pteronyssinus*; DF, *Dermatophagoides farinae*; RML, red mosquito larvae

with mammalian and pollen allergens. The sex of the patients influenced the results with timothy and Cladosporium, and age influenced the results with horse, mugwort and HDM. The diagnosis (asthma or rhinitis) significantly influenced the SPT with all allergens except Alternaria and shrimp.

Sensitization in relation to month of birth

When the month of birth was compared between patients having allergies against pollens, furred animals, HDM and insects no significant differences were found, neither when all atopic patients were analyzed, nor when children only were included in the analyses.

Discussion

In this study standardized allergen extracts with common inhalant allergens, as well as non-standardized allergen extracts with Cladosporium, Alternaria, cockroach, RML and shrimp, were used at 24 allergy clinics in Northern Europe and Asia for SPT on consecutive atopic patients with asthma and/or allergic rhinitis.

Although there is a rather good correlation between allergen specific serum-IgE and SPT,[7] an *in vitro* method (e.g. radioallergosorbent test, (RAST)), with analysis in one laboratory, might have diminished the problems with standardization in this multicenter study. However, *in vitro* tests would have been too expensive. Consequently, for evaluating the test results we used a standardized technique which minimized the influence of varying test techniques by different testing nurses. Thus, positive test reactions were recorded in accordance with the recommendations of the Standardization Committee of the Northern Society of Allergology: that is, the number of plus signs assigned to a positive reaction in an individual depends on the relation between the area of the wheal induced by the allergen and that induced by the positive histamine control in the same person.[4] By using this method, differences in test techniques among the participating clinics could be taken into account.

Faults caused by measurement errors should have been minimal because the wheals taped onto the records were measured by one person. We could not, however, control the precision when the wheals were outlined with a pen at the participating clinics.

Sensitization pattern

Looking at the whole group of patients, cat and two pollen allergens (timothy and birch pollen) were found to be the most important allergens. These results were in accordance with other studies on Swedish adult patients,[8,9] as well as studies on Swedish children.[10] Reports from other countries have shown HDM to be more important, for example, in London, England,[11] Sydney, Australia,[12] and Chicago, USA.[13] There are also studies from Scandinavian countries showing HDM to be most important: Bergen, Norway[14] and Copenhagen, Denmark.[15]

Positive reactions with inhalant insect allergens are usually not reported in Western allergy papers reporting sensitization rates in atopic patients. Our findings of positive skin tests with cockroach and RML in a considerable proportion of the atopic population raised the question of whether inhalant insect allergy constitutes an important problem in patients with asthma and rhinitis. Sensitization with cockroach had earlier been described in atopic patients in, for example, the USA[13] and with RML in Japan[16] and Sweden.[5,17] Multi-sensitization with different insect allergens seems to be common and cross-reactions exist among insects,[18] and between insects and crustaceans,[5] and probably also between insects and HDM.[19]

Sensitization at different clinics and in relation to patients' residences

It should be stressed that the differences in sensitization found between different centers in this study do not give a true measure of the prevalence of atopic sensitization in the general population at the respective centers; rather, they only show the relative importance of the different allergens in atopic patients.

The relative importance of furred animal allergens was highest among atopic patients in the most northern centers. This finding could be a reflection of the fact that mites and pollen are less important allergens in these regions.

Among the pollens, birch gave most positive SPT reactions in Göteborg, which matches the fact that pollen counts have shown high values for birch pollen in Göteborg compared with other regions.[20]

Mugwort plants are less abundant in Northern Sweden, Tromsö and Reykjavik than at the other Scandinavian places included in the study,[20,21] and for this reason, the finding of fewer positive SPT with this extract in the most Northern areas was to be expected. Mugwort allergy, according to our study, seems to be more important in Eastern Europe and Siberia than in Scandinavia, which is in accordance with aerobiological data.[21]

Mites are less often found in areas with low humidity during the winter, such as in the North in centers not close to the Atlantic, which explains the relatively low figures for positive tests with *D. pteronyssinus* and *D. farinae* in the Northern Swedish centers. The high frequency of sensitization against HDM found in Klaipeda can partly be explained if mite allergens cross-react with cockroaches.[19] Cross-reactions between arthropods[5,18] could also possibly explain why shrimp sensitization is most prevalent in Klaipeda, in spite of a very low consumption of shrimps in Lithuania. The question of cross-reactions among various groups of inhalant allergens will be discussed in another paper.

Positive SPT with Cladosporium and Alternaria were not common. The highest figures were found in children in Southern Sweden and the lowest figures in Siberia. Spore counting has shown that spore frequencies in outdoor air are almost equal in different Nordic countries, that Cladosporium is the most important spore type, and that Cladosporium frequencies decrease as one travels northwards.[22] The frequencies of Alternaria spores are four to five-fold lower in Nordic countries than in Central Europe.[22] SPT with Cladosporium and Alternaria, performed on patients from seven Western and Southern European countries, have shown positive reactions ranging from 3% (Portugal) to 20% (Spain).[23] The figures for positive SPT in our patients (mean 4–5%) are generally smaller. SPT results with mold should, however, be looked upon with caution, since biologically standardized test extracts are not available.

We did not find significant differences in sensitization patterns between town and countryside. In an earlier study performed on atopic farmers, Eriksson *et al.*[24] found that RML gave the highest number of positive SPT, followed by *D. pteronyssinus* and mugwort, while very few farmers were sensitized against timothy, birch, cat and dog. The present study, showing only a tendency to relatively more allergy against HDM in rural patients and more allergy against pollen and furred animals in urban patients, only partly corroborates these findings. It has been reported that farmers, due to heavy exposure, are often allergic to storage mites.[25] Thus, cross-reactions between storage mites and HDM might possibly explain a higher sensitization rate with HDM in rural patients. It is, however, obvious that factors other than allergen exposure are of importance for sensitization. An adjuvant factor favoring sensitization in cities and towns could be atmospheric pollution, originating, for example, from vehicle exhaust gases.[26]

Sensitization in relation to diagnosis, age and sex

Patients with only rhinitis were more often sensitized against tree and grass pollens, while those with only asthma more often showed sensitization against mites, furred animal dander, RML and Cladosporium. This has been described previously[8,12] and could be explained by the fact that the bigger pollen particles do not easily reach the bronchial tree, contrary to the smaller particles carrying the other allergens.

The relative incidence of positive SPT with mugwort and birch increased with age. The reason could be a decrease with age of the relative importance of several other allergens. A decrease with age, similar to the finding in this study, has earlier been reported with timothy, cat and horse.[8]

Our finding of a sex difference, with positive SPT with timothy and Cladosporium, for example, being more common in males than in females, is not easily understood. Similar sex differences regarding HDM[8,12,14,27] and timothy[8] have, however, earlier been reported. In a Dutch general population, men had lower prevalence than women regarding specific IgE to birch.[27] As far as furred animal dander allergy is concerned, some studies found male preponderance with cat in Norwegians[14] and with animal allergens in young but not in aged Danish people.[28] Intracutaneous testings on British asthmatic patients have shown an opposite sex difference, with more women having positive results with animals.[11] Sex differences might be explained by differences in environmental

exposure of women and men, or by hypothetical genetic differences. In our study, males showed a generally higher degree of atopy than females.

Mono-allergy and multi-allergy and degree of atopy

Among our atopic patients, 26% had a mono-allergy and 74% had an allergy against two or more allergens. The proportion of patients with multi-allergy decreased with age, which is in agreement with other studies[8,11,29] and could be regarded as a reflection of the general tendency towards a decreasing degree of atopy with age, which was also found in our study.

Relation to month of birth

We could not find any significant relationship between the patients' month of birth and their sensitization patterns. Although there are earlier studies which could not find any relationship between the sensitization pattern and month of birth,[30] several studies have shown a correlation between the month of birth and sensitization against pollens, particularly birch,[31] as well as mite[32] and animals.[33] One reason for our result could be the geographically scattered centers with different pollen seasons; for example, Reykjavik was almost without any deciduous trees and Vladivostok had low concentrations of these pollens.

Conclusion

It is concluded that sensitization to various inhalant allergens is influenced by geographical factors (presumably environmental exposure of allergens) and also by diagnosis (i.e. asthma and/or rhinitis), sex and age. We could not find any significant relation to month of birth in this study, which had many geographically widely separated centers.

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